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Abbreviations

BC=black carbon

CO=carbon monoxide

ECG=electrocardiogram

NO_2=nitrogen dioxide

O_3=ozone

$PM_{2.5}$ =particle mass <2.5 μg/m^3

SO_2=sulfur dioxide

TEOM=Tapered Element Oscillating Microbalance

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Abstract

Increased levels of daily ambient particle pollution have been associated with increased risk of cardiovascular morbidity. Black carbon (BC) is a measure of the traffic-related component of particles. We investigated associations between ambient pollution and ST-segment levels in a repeated measures study including 269 observations on 24 61-to-88 year-old active Boston residents each observed up to 12 times from June to September, 1999. The protocol involved continuous Holter ECG monitoring including 5 minutes of rest, 5 minutes of standing, 5 minutes of exercise outdoors, 5 minutes of recovery, and 20 cycles of paced breathing. Pollution-associated ST-depression was estimated for a 10th to 90th percentile change in BC. We calculated the average ST-segment level, referenced to the P-R isoelectric values, for each portion of the protocol. The mean BC level in the previous 12 hours, and the BC level 5 hours prior to testing, predicted ST-segment depression in most portions of the protocol, but the effect was strongest in the post-exercise periods. During post-exercise rest, an elevated BC level was associated with –0.1 mm ST-segment depression ($p=0.02$ for 12-h mean BC; $p=0.001$ for 5-h BC) in continuous models. Elevated black carbon also predicted increased risk of ST-segment depression $\geq$0.5 mm amongst those with at least one episode of that level of ST-segment depression. Carbon monoxide was not a confounder of this association. ST-segment depression, possibly representing myocardial ischemia or inflammation, is associated with increased exposure to particles whose predominant source is traffic.

Introduction

Numerous studies have demonstrated associations of acute increases in particle levels with increased risk of cardiac morbidity and mortality (Pope et al. 1995). Efforts have been directed toward understanding mechanisms for these associations. Canine studies showing increased risk of myocardial ischemia (Wellenius et al. 2003) and a chamber study showing decreased brachial artery diameter with particle exposure (Brook et al. 2002) have provided supportive evidence for particle-induced ischemia as a potential mechanism. Both carbon monoxide (CO) and particle mass <2.5 $\mu g/m^3$ ($PM_{2.5}$) were associated with increased risk of ST-segment depression during repeated submaximal exercise tests among subjects with coronary heart disease in 45 adults with stable coronary heart disease in Helsinki, Finland (Pekkanen et al. 2002). $PM_{2.5}$ was believed to be the primary source of this association, but because of correlation with CO, the authors reported that independent effects were difficult to separate. Black carbon (BC) may be a more precise measure than $PM_{2.5}$ of the portion of particle mass related to traffic (Laden et al. 2000). We examined whether there were independent associations of the ambient traffic-associated pollutants, BC and CO, with ST-segment depression before and after sub-maximal exercise in a community-based repeated measures study of elderly adults from Boston, Massachusetts.

Methods

Study Design and Protocol

We recruited a panel of elderly subjects living at or near an apartment complex located within a kilometer of a central site monitoring station. A baseline screening questionnaire was administered regarding medications, pulmonary and cardiac symptoms, and smoking

history. A resting 12-lead ECG was performed. Exclusion criteria included unstable angina, atrial flutter, atrial fibrillation, or paced rhythm. Each subject was assigned a day of the week and a time of day for weekly testing, with the goal of 12 weekly visits during the summer of 1999. Each week participants were administered a brief questionnaire regarding chest pain, medication changes and whether medications had been taken that morning. Continuous Holter monitoring with electrodes in a modified V5 and AVF position were performed using the Marquette Seer Digital Recorder (Marquette Inc, Milwaukee, WI). The protocol (Gold et al. 2000) consisted of: (1) Five minutes of rest. (2) Five minutes of standing. (3) Five minutes of exercise outdoors. If the participant felt able, a standard walk was performed, involving one climb up a slight incline. (4) Five minutes of supine recovery. (6) Three minutes, twenty seconds of slow, paced breathing. For each of 20 respiratory cycles, the participant was asked to breath in for 5 seconds and then out for 5 seconds, coached by a technician.

Processing of Holter Recordings

The digital Holter recordings were downloaded to a MARS ultra 60 playback system (Marquette Inc, Milwaukee, WI) for analysis. ST-segments were evaluated (1) for the average value for each portion of the protocol and (2) for possible ischemia, defined as reversible horizontal or downsloping ST-segment depression$\geq$ 0.5 mm, a level associated with adverse cardiac risk in patients with acute coronary syndrome (Cannon et al. 1997). Recordings were visually scanned by an experienced analyst to censor artifacts. Custom algorithms were created to calculate the average "ST-segment level" or value, referenced to the P-R isoelectric values, for each portion of the protocol. Separately, each candidate

episode of reversible ST-segment deviation was evaluated as possibly representing ischemia, by utilizing real-time ECG strips by an experienced analyst and physician blinded to air pollution status. A table of J-point values, ST-segment values, ST-segment slope, and heart rate was printed for each candidate episode beginning 10 minutes before each episode and ending 10 minutes after the resolution of each episode. The ST-segment value 60 msec after the J-point was used to define the ST-segment deviation and the ST slope.

Air Pollution Measurements

Air pollution measurements ($PM_{2.5}$, BC, CO) were collected at a central site within 0.5 kilometer of the residences of the subjects, which were on the same busy street trafficked by diesel-powered buses and trucks, as well as cars of commuters. Measurements of sulfur dioxide(SO_2), ozone(O_3), and nitrogen dioxide(NO_2) were obtained from state monitoring sites in Boston. Continuous $PM_{2.5}$ was measured using the Model 1400A Tapered Element Oscillating Microbalance (TEOM) (Rupprecht and Patashnick; Albany, NY). The TEOM sample filter is heated to 50°C, leading to season-specific temperature-related loss of semi-volatile mass. Season-specific calibration factors were used to correct for the losses of mass (Allen et al. 1997). The calibration factors were obtained by regressing continuous $PM_{2.5}$ concentrations averaged over 24-h periods on the corresponding collocated integrated 24-h Harvard Impactor low-volume Teflon filter gravimetric measurements.

In the summer in Boston, BC measurements are surrogates for carbonaceous particles, components of $PM_{2.5}$, many of which derive from traffic (local or transported). BC data from this instrument, using the internal empirically determined conversion

factor, has correlated well with elemental carbon (Hansen and Rosen 1984). BC was measured using a model AE-14 Aethalometer (Magee Scientific Inc., Berkeley CA). CO was measured continuously with a ThermoEnvironmental (Franklin, MA) Model 48 gas analyzer using a US EPA reference method.

Statistical Analyses

For each portion of the protocol, we analyzed the effect of pollution on between-visit, within-subject changes in mean ST-segment level. A standard model for analyzing repeated measures on the same individual is the linear mixed model, which accounts for residual correlation among observations taken on the same subject by including normally distributed random intercepts and pollutant slopes in a linear regression model. Descriptive statistics for ST- segment values, however, revealed skewness in the subjects' baseline values, making the normality assumption on the random intercepts untenable. As a result, we used two alternative approaches to analyzing the data from each portion of the protocol. First, treating ST-segment level as a continuous outcome, we used a conditional linear mixed model (Verbeke and Molenberghs 2000), which estimates the within-subject effect of a pollutant after conditioning out each subject's baseline value. This corresponds to putting subject into the linear model as a fixed effect, while specifying the linear slope of pollutant as a random effect (Verbeke and Molenberghs 2000).

The ULTRA study has demonstrated the importance of selecting a vulnerable population when seeking to investigate whether pollution influences ECG changes consistent with ischemia (Pekkanen et al. 2002). While we did not, as in the ULTRA study, have a cohort selected for coronary artery disease, our aim was to evaluate particle

pollution effects on elderly individuals with a tendency to develop ST-segment depression, with some ECG evidence for vulnerability to the outcome of interest. Therefore, a priori, for each part of the protocol for analyses treating ST-segment level as a continuous outcome, we only included vulnerable subjects, defined as those whose mean ST-segment values for that part of the protocol were negative at least two times during the study (23 of 28 study participants). Analyses were repeated including all study participants to assess the sensitivity of results to the exclusion criteria and to the presence of outliers.

In additional to analyses evaluating ST-segment level as a continuous outcome, we analyzed the binary response "ST-segment depression $\geq$0.5 mm", defined as a mean ST-segment level for a given portion of the protocol of at least -0.5 mm (i.e., mean ST-segment level lower than or equal to –0.5 mm, compared to ST-segment level higher than –0.5 mm). This definition differed from that of classic ischemia in that it did not require within-test or within-portion of the protocol reversibility. For this secondary analysis, we fit a logistic regression model with random intercepts to data from those subjects having at least one response of each type (depressed and non-depressed ST-segment) during that particular protocol (13 of 28 study participants contributed data to at least one portion of the protocol).

Twenty-four study participants with 269 observations were included either in analyses with continuous or with binary (dichotomous) ST-segment outcomes. We had sufficient observations to evaluate the effects of between-weekly-test increases in pollution levels on between-test depression in the mean ST-level for each portion of the protocol. However, we were unable to assess the effect of between-test changes in

pollution on the risk of within-test reversible ST-segment depression that fit criteria for ischemia, because of the rarity and lack of variability of such events. During the study only 5 of 28 study participants had ischemic ECG events (defined above as within-test reversible horizontal or downsloping ST-segment depression$\geq$ 0.5 mm).

Each regression model included an indicator variable for each subject, pollutant concentration, a cubic effect of the mean of the current hour temperature, and a linear trend of time. Other confounders considered included day of week and time of day, which were both highly correlated with the subject indicator variables, and were thus dropped from the model. Separate models were fit using lags of 1 to 24 hours, as well as previous 12 and 24 hour moving averages, of pollution concentration. Finally, models containing multiple pollutant concentration as predictors were fit to account for confounding due to moderate to high correlations among different pollutant concentrations. Multiple lags and moving averages were evaluated to select the best lag structure for temperature and each individual pollutant, and models reflect these evaluations. All statistical analyses were performed using the SAS statistical software package. The conditional linear mixed models were fit using PROC MIXED, whereas the logistic mixed models were fit using PROC NLMIXED (SAS Institute Inc. 1999).

Estimates of the effects of BC were scaled to the difference between the 10^{th} and the 90^{th} percentile in levels for the appropriate lag or mean value of BC.

Results

The median age of the population was 73, and many participants had cardiac risk factors (e.g., history of hypertension, prior smoking) or coronary artery disease (Table 1). As expected, mean heart rate rose during exercise and returned to baseline at rest (Table

2) during the 269 tests for the 24 participants included in analyses. Simultaneously, median ST-segment level was lower during and immediately after exercise than at first rest. ST-segment depression was rare in the modified AVF lead, and all subsequent analyses are based on findings in the modified V5 lead, the lead that most consistently identifies myocardial ischemia when it is present (Lanza et al. 1994). Air pollution levels were only modestly elevated, and maximum levels for EPA criteria pollutants were all below accepted or proposed National Air Quality Standards (Table 3)(www.epa.gov). CO levels never exceeded 2 ppm. BC levels rose early in the morning and were at their peak between 6 and 9 AM.

Individual hourly lag models showed consistent negative associations of ST-segment level with increased BC for the first 12 hours prior to testing (Figure 1), but with waning effects after 12 hours. The strongest association between BC and ST-segment level was for the 5-h lagged value of BC (Table 4). For each portion of the protocol in the continuous models, higher 5-h BC predicted lower between-test mean ST-segment levels. There was also a consistent effect of the mean of the BC levels during the 12 hours prior to testing, on between-test ST-segment depression. Higher BC levels were also associated with lower between-test ST-segment levels, when averaged (for each individual, for each testing session) over all portions of the protocol (estimated overall ST-segment change=-0.08 mm; p=0.03 for 12-h mean BC; estimated change =-0.10 mm; p=0.004 for 5-h BC), suggesting a pollution effect sustained throughout the protocol. While they were also consistently negative, associations of ST-segment depression with the mean of BC during the 24-h prior to testing were weaker; and the BC levels 2 days prior to testing had no association with ST-segment depression. There was

no effect of air pollution on changes in ST-segment level from the rest to exercise or from the exercise to recovery portions of the protocol. The effects of black carbon on ST-segment depression were not modified by medication use, diagnosis of coronary artery disease, hypertension, gender or ethnicity.

For the smaller group who had at least 0.5 mm depression at one or more visits, increases in BC were associated with an elevated risk of ST-segment depression $\geq$ 0.5 mm, though confidence in the estimates was limited by the smaller numbers of observations (Table 4). The largest estimated risk was during the rest period immediately after exercise, when there was a 10.4-fold risk (95% CI: 1.3, 83.0) of having between-test ST-segment depression $\geq$ 0.5 mm. While CO was associated with ST-segment depression in single pollutant models, in multiple pollution models, only black carbon remained associated with ST-segment depression (Table 5).

Discussion

In elderly subjects, we found that increases in levels of ambient black carbon in the 12 hours prior to testing were associated with between-week depression in the mean ST-segment levels that was present throughout the testing session, with the strongest effects occurring in the post-exercise recovery portions of the protocol, a period of cardiac vulnerability in patients with coronary artery disease (Frolkis et al. 2003). There was no effect of pollution on within-testing session changes in the magnitude of ST-segment depression. The risk of ST-segment depression of $\geq$ 0.5 mm was elevated with higher pollution; new ECG depression of this magnitude has been associated with increased risk of adverse cardiac events among patients with acute coronary syndrome (Cannon et al. 1997).

While we found pollution to be associated with ST-segment depression sustained throughout the testing session, the Finnish portion of the ULTRA study found associations of pollution with reversible exercise-induced ST-segment depression (Pekkanen et al. 2002). The etiology of the ST-segment depression we observed is unclear, but may represent the consequences of subclinical myocardial ischemia, inflammation, or both.

Although a minority of our subjects had documented coronary disease, many had risk factors predisposing them to subclinical disease and possible ischemia. Particle pollution may decrease myocardial oxygen supply and increase the risk of cardiac ischemia due to epicardial coronary disease through potentially interrelated mechanisms including: systemic inflammation, oxidative stress, endothelial dysfunction and/or autonomic dysfunction (Liao et al. 1999; Gold et al. 2000). Coronary artery disease is now considered, in large part, an inflammatory process (Ridker et al. 2000), and transient increases in air pollution could lead to transient exacerbation in vascular inflammation. Particle pollution has been linked to ST-segment changes in healthy canines (Godleski et al. 2000), and to reduction of the time to ischemic changes in canines with partial coronary artery occlusion (Wellenius et al. 2003). Brachial artery diameter, which is correlated with coronary artery diameter, was diminished in healthy subjects after exposure in a chamber to concentrated ambient particles (Brook et al. 2002), concomitant with elevated levels of endothelin.

Rather than causing subclinical ischemia, pollution-associated systemic inflammation may lead to low-grade myocardial inflammation, with associated subtle repolarization changes, including sustained ST-segment depression. A series of

epidemiologic studies have found associations of particle pollution with elevation of measures of systemic inflammation including plasma viscosity (Peters et al. 1997), fibrinogen (Gardner et al. 2000), neutrophil count, VCAM, ICAM (Salvi et al. 1999), and C-reactive protein (Peters et al. 2001).

In this same study, in the entire cohort, we found black carbon was associated with a decrease in heart rate variability, suggesting traffic-particle associated autonomic dysfunction (Schwartz et al. 2005(In Press)). Future work will focus whether ambient pollution leads to ST-segment depression and autonomic dysregulation through related pathways (e.g., inflammation) or through separate pathways.

Black carbon can be viewed as a surrogate for traffic-related particle pollution; exhaust emissions from diesel-powered vehicles have been identified as the main source of black or elemental carbon in urban areas (Schauer 1996; Janssen et al. 2002). Laden and coworkers, in a study of six US cities, found that traffic particles were more strongly associated with cardiovascular deaths than particles from coal burning (Laden et al. 2000). While BC influenced ST-segment depression, we did not find independent effects of CO on ST-segment level, perhaps because of the low levels of exposure. In one study, short-term exposure to CO, producing carboxyhemoglobin levels of 2-to 3.9 percent were associated with ischemic ST-segment changes in exercising subjects with coronary disease (Allred et al. 1989), though these low-level effects were not reproduced in a study by Sheps and colleagues (Sheps et al. 1987). ST-segment depression during exercise was associated with $PM_{2.5}$ and CO in the Finnish study of subjects with stable coronary heart disease who performed repeated biweekly submaximal exercise tests over a 6-month period (Pekkanen et al. 2002). In that study, correlation between the two pollutants made

it more difficult to separate their effects. In our Boston setting, CO was not an independent predictor of ST-segment depression. An alternative explanation for the lack of independent associations of the gases with ST-segment depression is more misclassification of exposure, particular since all the gases other than CO were measured at distances farther than the site where BC and $PM_{2.5}$ were measured, which was very close to the health effects testing site (see above).

This study was limited by lack of personal exposure measurements for carbon monoxide and particles. However ambient levels were measured on the same busy city street as the participant residences, less than 0.5 km away, and studies in Boston have shown that ambient concentrations are good surrogates of personal exposures to $PM_{2.5}$ of ambient origin (Rojas-Bracho et al. 2000). Moreover, the consequence of using ambient particle measures to estimate exposure is likely to be a modest underestimation of pollution effects (Zeger et al. 2000). Our ability to investigate interactions between participant characteristics such as beta-blocker use and particle effects was limited by the size of the population. Confidence in and generalizability of our estimates for our dichotomous outcome was limited by small numbers of observations. While our cohort was vulnerable on the basis of age, previous smoking, or hypertension history, our potential to document overt ischemic episodes was also limited by the choice of a population, only 18% of whom had diagnosed clinical coronary artery disease. Even in the ULTRA study of a population with doctor-diagnosed coronary artery disease subjected to submaximal exercise, sufficient episodes to examine the outcome of ischemia were documented only among Finnish participants, but not among participants from the two other countries (Pekkanen et al. 2002). Our primary analyses did include

one individual who, on 3 of 12 visits, reported smoking 1 to 3 cigarettes or cigarillos within the previous 48 hours. His data only met the inclusion criteria for examining the dichotomous ST-segment depression $\geq$ 0.5 mm during the exercise period; exclusion of this individual from analyses did not influence our findings. In our continuous analyses we only included those who we considered vulnerable on the basis of ST-segment depression (23 of 28). A sensitivity analysis showed that while inclusion of the entire cohort somewhat attenuated the magnitude and significance of the results, a significant association of 5-h black carbon with ST-segment depression was still detectable during the post-exercise period (second rest and paced breathing) (e.g., second rest effect estimates: –0.11 vs –0.08; p=0.001 vs 0.007 for subcohort with at least two episodes of ST-segment depression vs the entire cohort (233 vs 317 observations)).

Conclusion

In conclusion, in a population of elders susceptible to cardiovascular pollution effects on the basis of age or underlying cardiovascular disease, we found an association between traffic-related particles and ST-segment depression that may represent ischemia or myocardial inflammation.

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Table 1. Participant Characteristics

Characteristic	Entire Cohort (Total N=28) N	(%)	ST Segment Analysis Continuous Outcome[a] (Total N=23) N	(%)	ST Segment Analysis Dichotomous Outcome [b] (Total N=13) N	(%)
Sex						
Male	7	(25)	5	(22)	3	(23)
Female	21	(75)	18	(78)	10	(77)
Race/Ethnicity						
Black, Non-Hispanic	8	(29)	6	(26)	3	(23)
White	19	(68)	16	(70)	9	(69)
Other	1	(4)	1	(4)	1	(8)
Cigarette smoking						
Never	11	(39)	10	(43)	4	(31)
Former	16	(57)	13	(57)	8	(62)
Current	1	(4)	0		1	(8)
Ever Asthma [‡]	1	(4)	1	(4)	1	(8)
Coronary artery disease (Ever angina or heart attack)	5	(18)	5	(22)	4	(31)
Ever congestive heart failure	2	(7)	2	(9)	1	(8)
Ever hypertension [c]	11	(39)	10	(43)	5	(38)
Medication use						
B-blocker	5	(18)	4	(17)	1	(8)
Calcium channel blocker	3	(11)	3	(13)	2	(15)
Angiotensin-converting Enzyme inhibitor	7	(25)	7	(30)	4	(31)
Age (yrs): median (range)	73 (60-89)		71 (61-88)		76 (62-88)	

Percentages may not add up to 100 because of rounding.

[a] Analyses assess the association of pollution with ST segment level.

[b] Analyses assess the association of pollution with ST segment depression $\geq$ 0.5 mm.

[c] Report of doctor's diagnosis of disease.

Table 2. Median[a] Heart Rate and ST-Segment Level for 6 Protocol Periods

	First Rest	Blood Pressure	Standing	Exercise	Second Rest	Paced Breathing
Heart rate, beats/min	65 [b]	------	78	86	67	65
ST-segment level, modified V5 lead (mm)	-0.13	-0.10	-0.08	-0.29	-0.27	-0.17
ST-segment level, modified aVF lead (mm)	0.12	0.12	0.11	0.10	0.05	0.10

[a] Median of the mean values for each part of the protocol, for observations included in analyses. Based on 269 observations on the 24 subjects in analyses using either the continuous or dichotomous outcomes.

[b] Median heart rate for the period that includes both first rest and blood pressure portions of the protocol.

Table 3. Ambient Pollution[a] and Temperature Levels During Holter Monitoring

Pollutant (N=269)	10th Percentile	50th Percentile	90th Percentile	Maximum
Black carbon, μg/m^3				
5-h [b]	0.66	1.28	2.25	4.34
12-h mean [c]	0.79	1.14	1.68	2.23
$PM_{2.5}$, μg/m^3				
5-h [b]	3.8	9.5	25.6	41.0
12-h mean	4.1	9.8	25.9	35.6
CO, ppm				
5-h [b]	0.20	0.53	1.08	1.55
12-h mean	0.38	0.56	0.81	1.04
O_3, ppb				
1-h	8.5	27.1	54.9	95.4
5-h [b]	2.9	13.3	28.8	57.7
12-h mean	8.2	19.7	34.2	58.9
NO_2, ppb				
5-h [b]	11.9	22.4	35.6	53.1
12-h mean	14.3	21.4	35.2	48.9
SO_2, ppb				
5-h [b]	1.3	3.5	8.6	17.4
12-h mean	2.0	4.3	6.5	11.5
Temperature, °C	17.2	23.3	28.9	33.3

[a] Pollutants include daily black carbon, particulate matter with an aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$), ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and carbon monoxide (CO). Temperature is current 1-h mean.

[b] The distribution of the levels (Total N=269) during the 5th hour before Holter monitoring.

[c] The mean of the levels during the 24 hours before Holter monitoring.

Table 4. Ambient Black Carbon as a Predictor of ST-Segment Level for 5 Protocol Periods

Outcome Variable	N (obs)	5-h Black carbon (μg/m^3) Estimated ST-segment change (95% CI)[b]	P-value	12 h Mean Black carbon (μg/m^3) Estimated ST-segment change (95% CI)	P-value
ST-segment level, continuous [a]					
First rest	207	-0.11 (-0.20, -0.02)	0.02	-0.10 (-0.19, -0.01)	0.03
Blood pressure	209	-0.09 (-0.16, -0.01)	0.02	-0.08 (-0.15, -0.01)	0.03
Standing	196	-0.11 (-0.21, -0.01)	0.03	-0.09 (-0.19, 0.01)	0.09
Exercise	257	-0.08 (-0.17, 0.00)	0.06	-0.02 (-0.11, 0.06)	0.57
Second rest	233	-0.11 (-0.18, -0.05)	0.001	-0.07 (-0.14, -0.01)	0.03
Paced breathing	219	-0.11 (-0.17, -0.04)	0.001	-0.08 (-0.14, -0.01)	0.02
ST-segment depression ≥0.5 mm		**Estimated RR (95% CI)**		**Estimated RR (95% CI)**	
First rest	90 (29)[c]	5.1 (0.9, 28.0)	0.06	3.8 (0.7, 21.3)	0.11
Blood pressure	66 (22)	6.0 (0.8, 44.8)	0.07	5.7 (0.6, 56.3)	0.11
Standing	66 (28)	9.2 (1.1, 78.3)	0.05	8.3 (0.8, 81.9)	0.06
Exercise	114(38)	0.9 (0.2, 4.7)	0.86	0.6 (0.1, 3.1)	0.53
Second rest	90 (48)	10.4 (1.3, 83.0)	0.03	2.8 (0.5, 14.3)	0.19
Paced breathing	66 (22)	6.6 (0.9, 50.0)	0.06	3.5 (0.5, 23.6)	0.15

[a] Repeated measures regression models contain pollution concentration, a cubic effect of current temperature, and a linear trend of time.

[b] Estimated for a 10th-to-90th percentile change in black carbon.

[c] Numbers in parentheses represent the number of positive envents with ST-depression ≥0.5 mm

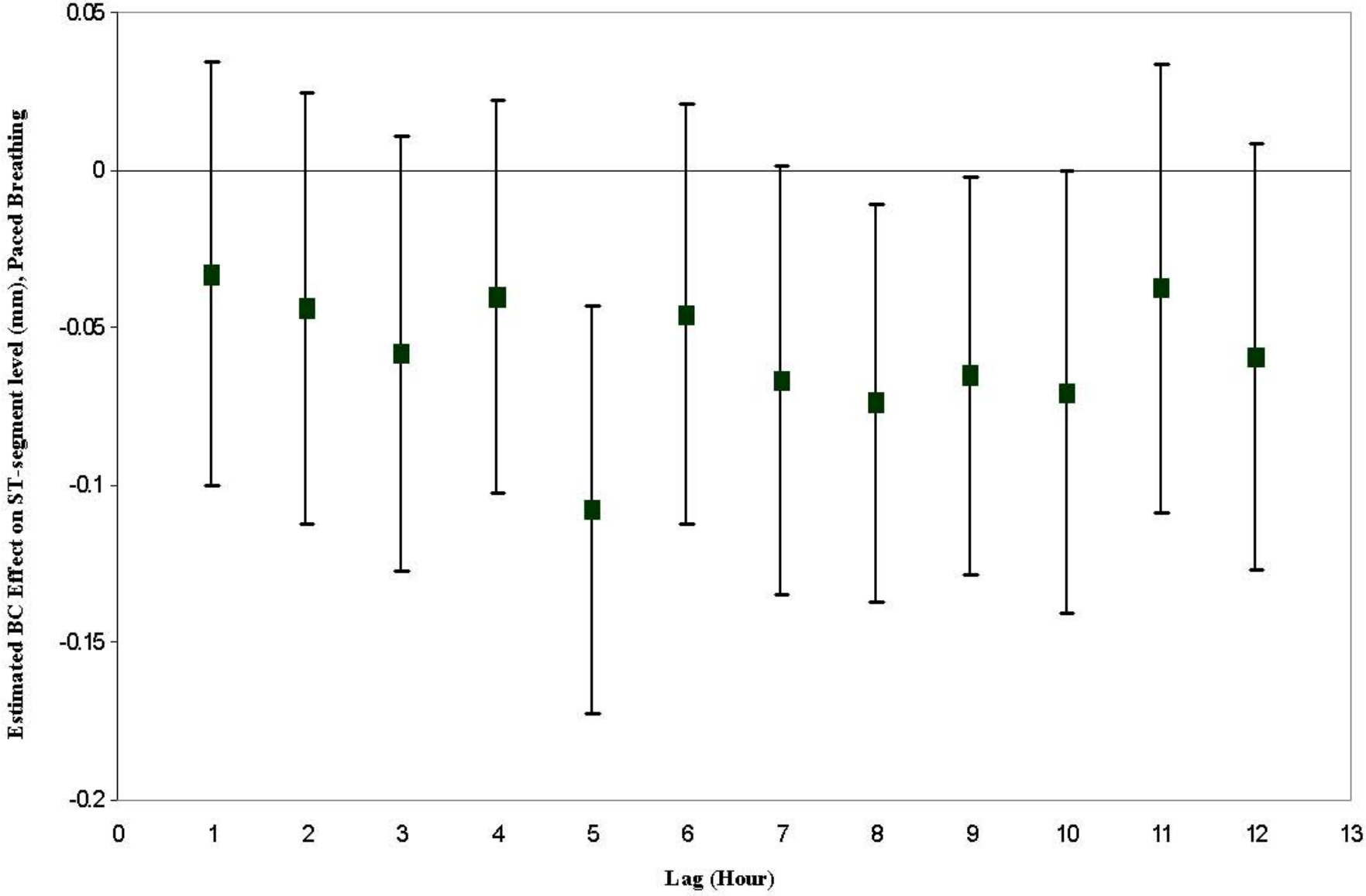
Table 5. Black Carbon and Carbon Monoxide as Predictors of ST-Segment Level in Single and Multiple Pollutant Models [a,b]

Outcome Variable	Model	Predictor Variable	Coefficient	Estimated Effect (95% CI)	P-value
ST-segment level, continuous					
Second rest	1	5-h Black Carbon	-0.07	-0.11 (-0.17, -0.05)	0.001
	2	5-h Carbon Monoxide	-0.15	-0.13 (-0.22, -0.04)	0.007
	3	5-h Black Carbon	-0.06	-0.09 (-0.17, 0.03)	0.04
		5-h Carbon Monoxide	-0.05	-0.05 (-0.17, 0.07)	0.45
	4	5-h $PM_{2.5}$	-0.0002	-0.004 (-0.08, 0.07)	0.92
	5	5-h O_3	1.38	0.04 (-0.05, 0.12)	0.39
	6	5-h NO_2	-1.96	-0.05 (-0.12, 0.03)	0.22
	7	5-h SO_2	-3.19	-0.02 (-0.10, 0.05)	0.53
Paced Breathing	1	5-h Black Carbon	-0.07	-0.11 (-0.17, -0.04)	0.001
	2	5-h Carbon Monoxide	-0.11	-0.09 (-0.19, -0.00)	0.05
	3	5-h Black Carbon	-0.07	-0.11 (-0.20, -0.03)	0.01
		5-h Carbon Monoxide	0.01	0.01 (-0.11, 0.13)	0.87
	4	5-h $PM_{2.5}$	-0.0008	-0.02 (-0.09, 0.05)	0.64
	5	5-h O_3	0.85	0.02 (-0.06, 0.11)	0.60
	6	5-h NO_2	-1.54	-0.04 (-0.11, 0.04)	0.33
	7	5-h SO_2	-5.15	-0.04 (-0.11, 0.03)	0.30

[a] Repeated measures regression models contain pollution concentration, a cubic effect of current temperature, and a linear trend of time. With the exception of Model 3, all other Models include only the single pollutant described. Model 3, for second rest and for paced breathing, includes both black carbon and carbon monoxide. Thus the coefficient for black carbon is adjusted for carbon monoxide.

[b] Estimated for a 10th-to-90th percentile change in black carbon.

Figure 1. Estimates (± 95% confidence intervals) of the effects of black carbon on mean ST-segment level during paced breathing, scaled to the difference between the 10th and the 90th percentile in levels for individual hourly lags.


0.05
0
-0.05
-0.1
-0.15
-0.2
Estimated BC Effect on ST-segment level (mm), Paced Breathing
0
1
2
3
4
5
6
7
8
9
10
11
12
13
Lag (Hour)